Remarks

The various parts of the Office Action (and other matters, if any) are discussed below under appropriate headings.

Claim Rejections - 35 USC § 112

Claims 1-16 were rejected as being directed to non-statutory subject matter. This rejection is moot with respect to claims 14 and 15 which have been cancelled.

In response to the comments submitted on March 19, 2008, the Examiner contends that a score residing in a computer buffer is not tangible to the practitioner of the method and cannot be realized **by the practitioner** until the score is further acted upon. The basis for these alleged requirements that the score be tangible **to the practitioner** and realized by **by the practitioner** is not understood. Storage of data in a computer buffer or memory clearly is a tangible (physical) event.

Regarding U.S. Patent No. 6,996,476, the Examiner states that the comparison is inaccurate, adding

> The presented claim from the '476 patent employs an analysis step that involves independent component analysis (ICA). ICA is an inherently graphical method that, as indicated by the presented claim, presents data as clusters."

To the contrary, ICA is a statistical and computational technique for revealing hidden factors that underlie sets of random variables, measurements, or signals. Perhaps the Examiner has been mislead by the term "clusters" and assumed that these are graphically represented. Nothing in the '476 patent has been found to suggest this. Rather, as understood the “clusters” are clusters or groupings of data. The Examiner’s attention is invited to Paragraph [0089] (for example) of the '476 patent to facilitate an understanding what ICA is actually about.

The Examiner concludes his argument by stating that "ICA of the '476 patent is not comparable to the score produced by the instant claims". We agree - ICA is a mathematical technique, whereas the score produced by the instant claims is a tangible, real world result enabling the comparison of molecules to be performed more accurately than in the prior art (see the discussion of this point in page 8, lines 1-20 of the present application).

The Examiner continues the statutory subject-matter objection (paragraph spanning pages 4 and 5 of the office action), referring to claim 13, which now recites "a computer interpretable recording medium bearing a set of instructions executable by a computer for carrying out the process of claim 1". The Examiner makes reference to page 9, lines 13-21. The reference passage states that "a computer interpretable medium… may be a signal carrier medium [such as a signal on a wire]…[and]…may also be a recording medium [such as a magnetic storage medium]". The former (a carrier medium) is presently considered objectionable but claim 13 now is explicitly directed to the latter ("a computer interpretable recording medium"). The specification does not state that a recording medium may also be a carrier signal. This is not what is taught by the description. The description in page 9, lines 13-21 both positively supports an interpretation of the "computer interpretable recording medium" of claim 13 as a magnetic or optical storage medium and positively supports an interpretation as not a signal carrier medium.

Claim Rejections - 35 USC § 102 and § 103

Turning now to the obviousness rejection, the Examiner appears not yet to appreciate the difference between the claimed method and the prior art (specifically, the Ashworth document).

In the argumentation presented on pages 6, 7 and 9 of the Office Action with regard to claim 1, the Examiner persists in referring to comparisons between sets of "field points", e.g. "determining a second molecule's field points in relation to that of the first molecule" (page 9, lines 5-6). However in the "Response to Arguments" section, the Examiner argues that this is justified in view of page 7, lines 10-16 of the specification. Here the Examiner paraphrases part of this portion as "field sample values are field points of the second molecule, though not necessarily field extremes". On this basis the Examiner substitutes "field points of the second molecule" into claim 1, in order to better fit his arguments with regard to Ashworth.

To do this however is thoroughly baseless, since the very next sentence of the description (page 7, lines 15-16) clarifies that "although the field sample values form a set of field points, this is not in the conventional sense of a field point representation of a molecule's extrema". It is thus submitted that the skilled person reading claim 1 would not substitute "field points of the second molecule" into claim 1 as the Examiner has done, both in view of the fact that the description explicitly cautions against the conventional understanding of "field points" when that term is used in the sentence cited

by the Examiner and because claim 1 uses the term "field sample values" with reference to the second molecule, not "field points".

To reiterate, the true language of claim 1 recites the step of: "determining at the position of each of the field points of the first molecule the field of a second molecule to obtain a set of field sample values".

Thus, in the claimed method, at this step the known field points at known corresponding field point positions of the first molecule are taken and field sample values for the second molecule, at those field point positions of the first molecule, are determined. No interaction between the electrostatic fields of the two molecules is considered at this step – rather a set of position information is used to determine a set of field sample values.

By contrast, in the method disclosed by Ashworth the field points of a first molecule are "fitted into a pharmacophore", measuring the resulting energy of overlay (page 4, lines 29-33). Since a pharmacophore is a 3-D array of field points (page 4, lines 22-23), it will be appreciated that the Ashworth method involves taking two known sets of field points and then determining the energy of overlay between those juxtaposed sets. At no stage has Ashworth been found to disclose determining the field of a second molecule at the position of each of the field points of a first molecule.

The Examiner argues (page 10, lines 3-6) that Ashworth "shows that a pharmacophore is determined which comprises a 3-dimensional array of field points defining a shape and volume of the field points derived from a plurality of molecules, reading on [to] obtaining a set of sample field values (page 4, lines 22-26)". Issue is taken with this contention, since Ashworth does not teach that the pharmacophore is determined "at the position of each of the field points of the first molecule" as would be necessary for this to read onto claim 1. Instead, as set out above, it is clear that in Ashworth two known sets of field points (that obtained in step (i), page 4, lines 29-30 and the pharmacophore) are overlayed, to then measure the energy of overlay (step (ii) in page 4, lines 31-33).

The Examiner appears to have misread what is disclosed by page 4, lines 22-26 of Ashworth. What Ashworth states is that [the set of field points in the pharmacophore] "is the aggregate average of the filed points derived from a plurality of molecules". The only reasonable interpretation of this is that the field points of a plurality of molecules are generated, and then the "aggregate average" of these field points is determined and used as the pharmacophore. This point is made clear on page 12, lines 29-31 of

Ashworth which states that "[a] pharmacophore is then generated by combining the field points of the "active" conformations". It is nowhere suggested in Ashworth that this combination process involves a re-sampling of the fields of any of the molecules involved - the pharmacophore generation process uses only the field points of the input molecules and not their fields. The fact that Ashworth then gives as one of the parameters for this process "the area over which a field point is averaged" (page 12, lines 31-32) supports this.

It is therefore wrong to assert that Ashworth discloses "determining at the position of each of the field points of the first molecule the field of a second molecule to obtain a set of field sample values".

This difference is not insignificant. As explained in page 7, line 22 to page 8, line 20, this step enables the claimed method to take better account of the shape of the electrostatic field associated with a molecule under consideration. For this reason, it is submitted that the method of claim 1 is inventive is not rendered obvious in view of the cited prior art.

To help illustrate the differences between the prior art approach and applicants' method described in the present application, attached are a sketch (applicants' method vs. prior art) and a diagram (pharmacophore generation in Ashworth).

The diagram of pharacophore generation in Ashworth illustrates what Ashworth teaches and why this is not relevant.

In the sketch, the upper half shows the prior art method of overlaying two sets of field points and then calculating the energy of overlay. The lower half illustrates the method of taking the positions of the field points of a first molecule and determining field sample values of the field of the second molecule at those positions. A further point to note with reference to the sketch is that in the prior art method the field points remain of fixed size regardless of the orientation of the overlay. In other words, if one aligned molecule 1 and molecule 2 slightly differently, one would use exactly the same field points in computing the score for that alignment. However, using a different alignment changes the sampling positions and hence the magnitude of the "field sample values".

A more mathematical way of expressing this latter point is that Ashworth's score is a function of the field point values (which are fixed), and the relative alignment of the molecules. The values and the alignment are independent. Hence "Ashworth Score" = f (values, alignment). However, applicants' values (the field sample values) are a

function of the alignment, which changes things dramatically. Hence "Applicants' Score" = f (values(alignment), alignment).

Conclusion

In view of the foregoing, request is made for timely issuance of a notice of allowance.

Respectfully submitted,

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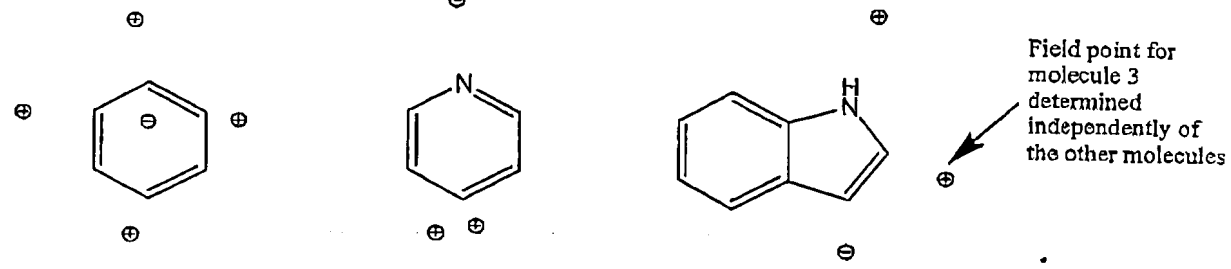
Pharmacophore generation process as described in Ashworth

Active conformation of Molecule 1

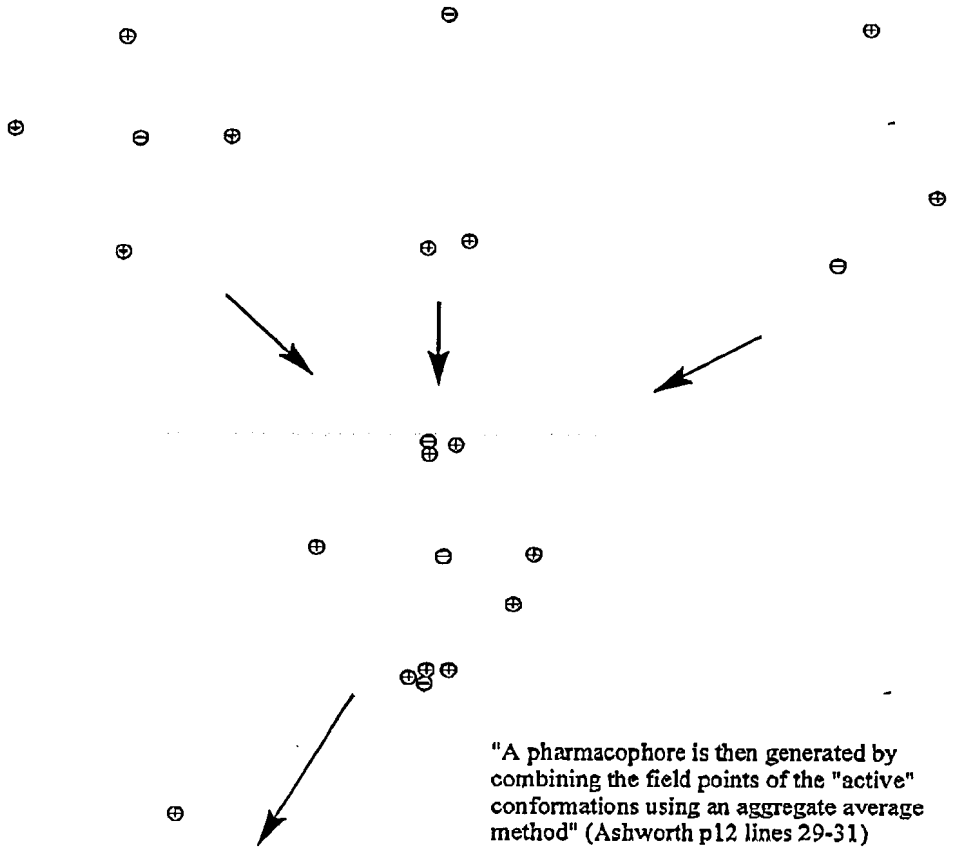
Active conformation of Molecule 2

Active conformation of Molecule 3

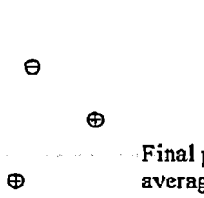


Field point for molecule 3 determined independently of the other molecules

"Field points for each conformation which lies on the optimum cyclic path are thus known" (Ashworth p12 lines 25-26):

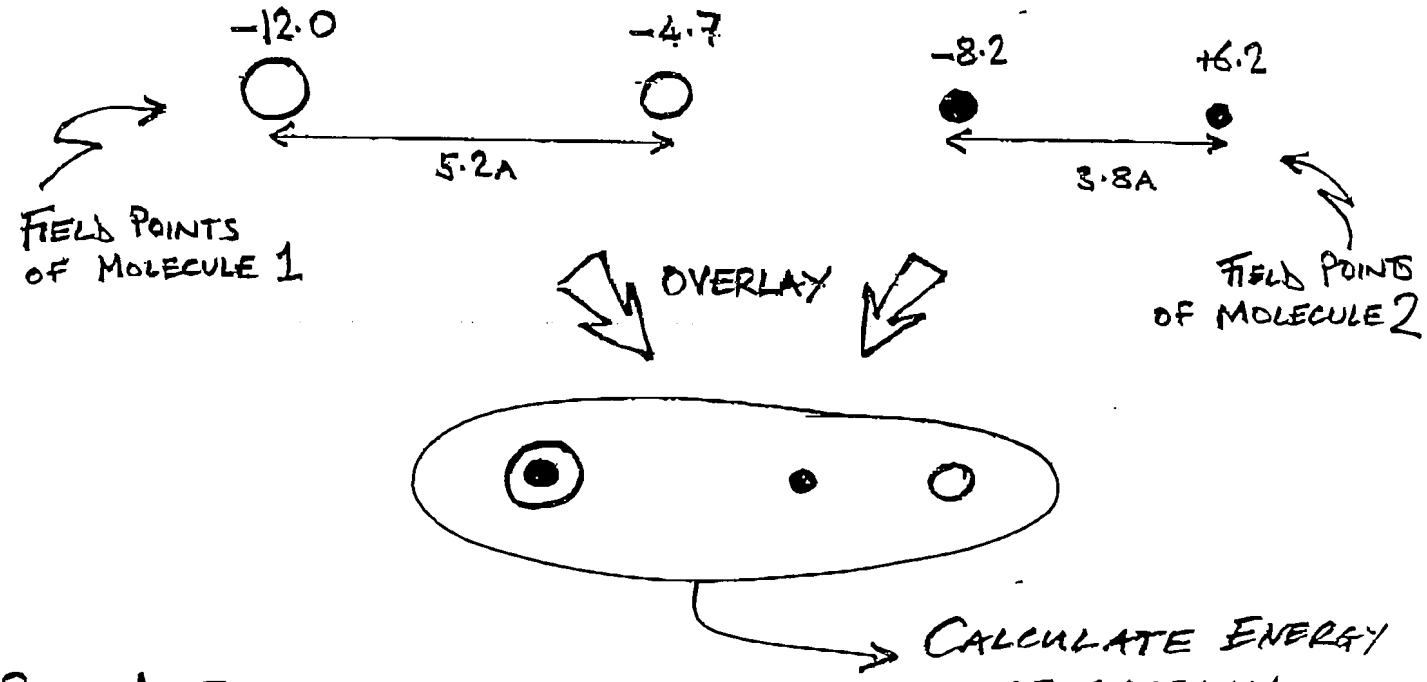


"A pharmacophore is then generated by combining the field points of the "active" conformations using an aggregate average method" (Ashworth p12 lines 29-31)



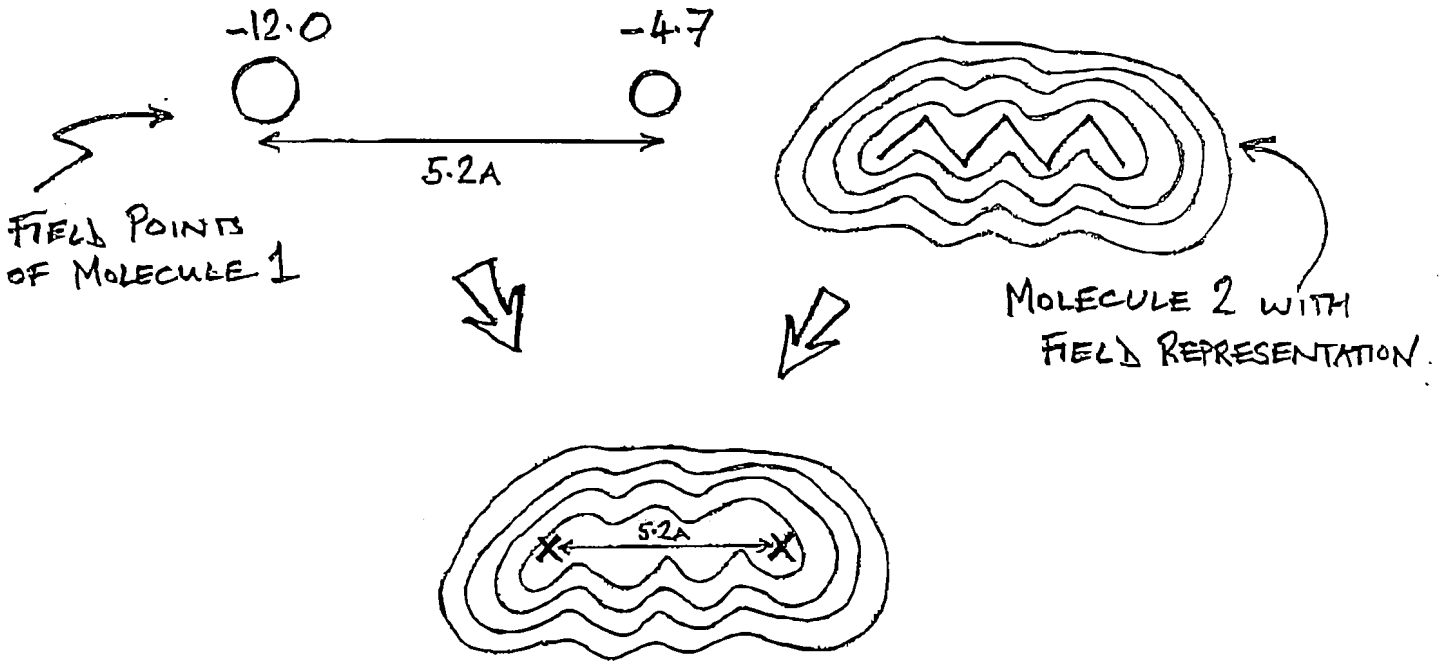
Final pharmacophore. Note that the aggregate average method (not fully described) is explicitly said to be performed on the field points of the input molecules. No reference is made at this stage to the underlying fields of the input molecules.

GRAPHICAL REPRESENTATION OF DIFFERENCE BETWEEN PRESENT INVENTION AND PRIOR ART



PRIOR ART

INVENTION



DETERMINE FIELD SAMPLE VALUES AT POSITIONS OF MOLECULE 1 FIELD POINTS